Liang aids hurricane victims

About 6:00 p.m. on Aug. 24, Stephen Y. Liang, MD, MPH, an assistant professor of medicine, division of infectious diseases and division of emergency medicine at Washington University School of Medicine in St. Louis, received a text alerting him to prepare for possible deployment to Texas. Hurricane Harvey had just begun its assault on the Gulf Coast, and days of rain and flooding were still to come. By 7:30 p.m. the order was confirmed, and by 11:30 that night Liang had packed his bags, kissed his wife and four children goodbye and arrived in Columbia, MO, ready to deploy as a member of the search-and-rescue team Missouri Task Force 1.

Stephen Liang is one of at least five Washington University faculty and staff who dropped everything to help victims of this year’s historically disastrous hurricane season. Jacob Keeperman, MD, assistant professor of anesthesiology and of emergency medicine, worked for a company that sent helicopter emergency medical services to Texas during Hurricane Harvey; Douglas Char, MD, professor of emergency medicine, was called to Texas and then Washington to help oversee the medical response to Hurricanes Harvey and Irma; and Jim Fehr, MD, professor of anesthesiology and of pediatrics, and Ty Davison, director of emergency management and business continuity, deployed to Puerto Rico in the aftermath of Hurricane Maria.

While they were away, their colleagues pulled together to keep operations on the Medical Campus running as normal. “Sometimes people forget about all the help that’s provided back home,” Keeperman said. “We could never have gone if we didn’t have colleagues who picked up the slack and covered our shifts. They contributed to the hurricane response effort, too.”

Liang is a member of Missouri Task Force 1, part of the Federal Emergency Management Agency’s (FEMA) National Urban Search & Rescue Response System. The team trains year-round so its members are prepared to respond within hours for just such a disaster.
After leaving WUSTL in 2014, I took a job as the Deputy State Epidemiologist at the Hawaii State Department of Health in Honolulu; while there, I had the opportunity to work on a variety of outbreak responses, such as the hepatitis A outbreak related to consumption of raw imported tuna (at the time the second largest HAV outbreak in recent US history), an island-wide outbreak of dengue fever on the Big Island of Hawaii, and hepatitis associated with consumption of a weight-loss herbal product.

My work also included developing antibiotic stewardship capacity through a state antibiotic stewardship collaborative, statewide Ebola preparedness, hurricane preparedness and response, legislative briefings, and smaller but no less important issues such as multiple measles introductions and angiostrongyliasis.

While in Hawaii, my husband and I took advantage of the ocean swimming, snorkeling, diving, hiking, and the marvelous good food, as well as the opportunity for a scenic beach wedding in 2014.

In 2017, we relocated to the East Coast to be closer to my elderly parents and I took a position as the Deputy Director of the Richmond City Health District in Richmond, VA. This position is primarily administrative, including oversight of clinical services at the health district (e.g., STI, TB, refugee health) and oversight of ST / HIV prevention, epidemiology, and emergency preparedness programs. Current areas of focus for me include working with state and city partners on responding to the opioid crisis, facilitating the move to a population-health based model for the health district, and driving the use of local data in our agency to facilitate informed decision-making.

I am continually surprised at how beneficial my ID fellowship training has been, even outside the realm of communicable disease and communicable disease epidemiology, and am grateful to staff and attendings for my experiences at WUSTL.
awards & announcements

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Jennie H. Kwon, DO, MSCI recently accepted a national position with the Society for Healthcare Epidemiology of America (SHEA). Jennie was appointed membership to the SHEA Research Network Review Committee for a three year term.

Rupa Patel, MD, MPH, DTM&H was named on the St. Louis Business Journals “2018 40 under 40” honoree list. In February 2018, the St. Louis Business Journal will introduce a class of 40 young professionals who are already making their mark on the local business community. A dinner event will be held on February 22, 2018 to honor these 40 professionals.

congratulations. . .

Peter U. Fischer, PhD who was recently promoted to Professor of Medicine.

Dr. Fischer’s research interest involves medical helminthology, especially filariasis and other neglected tropical diseases caused by parasitic worms. He has performed extensive field research on the diagnosis, epidemiology and control of filarial parasites in many countries in Asia and Africa. He has conducted basic laboratory research on filarial nematodes and their endobacterial symbionts and developed molecular diagnostic tests for filarial parasites. Dr. Fischer is an Adjunct Professor at the Department of Parasitology, Faculty of Medicine, University of Indonesia, Jakarta. He currently works with Dr. Gary Weil on the Bill and Melinda Gates Foundation-funded DOLF (death to onchocerciasis and lymphatic filariasis) project and studies alternative filariasis treatment strategies in large scale community trials. Dr. Fischer also studies North American paragonimiasis in Missouri to improve diagnostics for paragonimiasis globally.
awards

The Distinguished Faculty awards recognize outstanding achievements in clinical care, community service, research and teaching. They are co-sponsored by the dean’s office, the Office of Faculty Affairs, Central Administration and the Executive Committee of the Faculty Council.

Distinguished Clinician Award - 2017

Thomas C. Bailey, MD, professor of medicine, was honored for his outstanding contributions to the care of patients with infectious diseases (ID). A recognized expert in the field of mycobacterial diseases, Bailey’s compassionate manner, superb clinical diagnostic skills and generosity of spirit are the hallmarks of his approach to the complex care of patients needing multi-faceted and coordinated treatment. Dr. Bailey is the director of the ID clinic at Washington University School of Medicine (WUSM).

With a particular interest and expertise in tuberculosis, Bailey has served as the medical director for the Tuberculosis Program at the Saint Louis County Department of Health for more than 20 years. He has worked to enhance and automate state-mandated TB infection and disease reporting, which assists the health departments in their duty to initiate contact investigations and prevent the spread of TB. A strong role model and mentor for both faculty and fellows within the division of infectious diseases, Dr. Bailey successfully advocated for keeping tuberculosis as part of the medical school curriculum. He regularly offers relevant lectures about TB to fellows as well as area nurses and community groups.

Dr. Bailey has undertaken several leadership roles that have led to improved patient safety and medical outcomes. He oversees the proper use of antimicrobials throughout BJC HealthCare and serves as chair of both the Barnes-Jewish Hospital Antibiotic Utilization Review Committee and the BJC Anti-Infective Panel.

Dr. Bailey completed both his residency and a fellowship in ID at WUSM and joined the faculty in 1991.

Distinguished Educator Award - 2017

Steven J. Lawrence, MD, MSc, associate professor of medicine in the division of infectious diseases, is honored for his outstanding efforts to enhance medical education.

Lawrence has immersed himself in creating interactive curriculum materials and engaging educational programs related to infectious diseases, infection control, disaster preparedness and bioterrorism prevention. A respected clinician-educator, Lawrence worked hand in hand with medical students to improve retention and understanding of complex infectious diseases information through the use of emerging computer-based, self-learning study aids such as Anki. He also facilitated the use of small study groups and established new methods for student evaluations. Lawrence is the recipient of numerous teaching awards across the medical center and recently was awarded the Jerome T. Loeb Teaching Fellow Scholarship to further his efforts with dynamic curriculum development.

Often described as engaging and witty by students, faculty and patients, Lawrence is a dedicated continued
Lawrence and Kirmani Receive 2016-17 Distinguished Service Teaching Awards

Steven J. Lawrence, MD, MSc, associate professor of medicine, and Nigar Kirmani, MD, professor of medicine, were selected by the medical student class of 2019 to receive this year’s Distinguished Service Teaching Award. The distinguished service teaching awards are presented by Washington University medical students to faculty and house staff in appreciation of exemplary service in medical student education. Initiated by students and implemented with support from the Office of Medical Student Education, the awards honor Washington University educators who have made the most significant contributions to the training of future physicians.

The Clinical Department of the Year Award was accepted by Victoria J. Fraser, MD, Chair of the Department of Internal Medicine.

Dr. Lawrence earned his medical degree from Washington University School of Medicine in 1997 and a master’s of science degree in epidemiology from the University of London School of Hygiene and Tropical Medicine. He completed both his residency and fellowship in infectious diseases as well as served as a staff scientist in the division of infectious diseases at Washington University before joining the faculty as an instructor in 2005.
In 2017, Matt Kuhlmann, MD, instructor of medicine, left his role as medical director of the infectious diseases clinic to turn his focus on his research. Thomas C. Bailey, MD, professor of medicine, stepped in as the clinic director while continuing his role as medical director of Tuberculosis Control for St. Louis County. Dr. Bailey also has several leadership roles that have led to improved patient safety and medical outcomes.

E-P Barrette, MD, associate professor of medicine, became the medical director of HIV/Virology services for infectious diseases. Dr. Barrette has provided primary care to patients with HIV for 25 years and was formerly the medical director of the Primary Care Medicine Clinic in the Center for Outpatient Health at Barnes Jewish Hospital.

In July, the ID clinic expanded services to include evaluation and treatment of patients who are mono-infected with Hepatitis C Virus (HCV). The Infectious Diseases clinic offers comprehensive management of HCV, including HIV/HCV dual infections, from initial workup to treatment and monitoring. The ID clinic encompasses over 30 years’ experience in antiretroviral therapy and our ID physicians and staff have been treating dual infection with HIV and Hepatitis C for the past 5+ years. “We are a full team comprised of infectious disease specialists, an infectious disease pharmacist, and a nurse,” says Lemuel Non, instructor in medicine and lead attending physician of HCV patients. “ID clinic specialists welcome the opportunity to see patients with Hepatitis C.”

faculty highlights continued

Jeff Henderson, MD, PhD named co-director of new graduate program in the Division of Biology and Biomedical Sciences

Jeffrey P. Henderson, MD, PhD, assistant professor of medicine and molecular microbiology was recently selected as the co-director of the new Biochemistry, Biophysics and Structural Biology (BBSB) Graduate Program in the Division of Biology and Biomedical Sciences. Dr. Henderson did his infectious diseases fellowship here, at Washington University School of Medicine and has been faculty since 2006. Dr. Henderson will co-direct with Daved H. Fremont, PhD, professor of pathology and immunology, biochemistry and molecular biophysics and molecular microbiology.

The new BBSB program encompasses three related research areas, biochemistry, biophysics, and structural biology.
William G. Powderly, MD, was installed as the Larry J. Shapiro Director of the Institute for Public Health during a ceremony on September 27, 2017 at the Eric P. Newman Education Center. Dr. Powderly is also the Dr. J. William Campbell Professor of Medicine and co-director of the Division of Infectious Diseases at the School of Medicine.

The installation ceremony included presentations by Larry J. Shapiro, former executive vice chancellor for medical affairs and dean of the School of Medicine; Steve Lipstein, chief executive officer of BJC HealthCare; and Chancellor Mark S. Wrighton.

The directorship was named through the generosity of St. Louis-based BJC HealthCare, which has an enduring relationship with the university. Washington University physicians treat patients at Barnes-Jewish and St. Louis Children’s hospitals, each part of BJC HealthCare.

Dr. Powderly was joined by his wife, Betsy Keath, PhD and their daughter, Ailis, who traveled from Ireland to attend the ceremony.

Click here to view the installation Facebook photo album.

View a video of the installation ceremony.
Escota selected Clerkship Director in Medicine

Gerome V. Escota, MD, has been selected as the next Clerkship Director in Medicine. He will provide the professional, administrative and educational leadership for the third-year clerkship and sub-internship.

Dr. Escota is currently an Assistant Professor of Medicine and clinical faculty in the Division of Infectious Diseases. He also serves as Associate Program Director for the Infectious Diseases Fellowship Program. He has won numerous academic awards, including for his exceptional knowledge in Medicine, for teaching at the resident level and as a faculty member. Four months ago, he was the inaugural recipient of the J. Russell Little MD Clinical Education Award. This award is chosen by fellows and given to an Infectious Diseases faculty member for outstanding teaching.

Dr. Escota is also an excellent researcher who specializes in the study of the aging HIV-infected population and an outstanding clinician who has a track record of successfully mentoring fellows, residents and students in Infectious Disease and Internal Medicine. He is deeply invested in medical education, curricular design and pedagogy and in working towards bringing innovation into the medical school curriculum to maintain the preeminent role of the Department of Medicine in the education of medical students.

The clerkship director is an essential academic leader in the education of medical students on clinical rotation. He will begin as Clerkship Director starting March 1, 2018. We welcome Dr. Escota to his new leadership role in Medical Education.

-Melvin Blanchard, MD, FACP, Professor of Medicine
Chief, Division of Medical Education
Director, Internal Medicine Residency Program

Infectious Diseases Society of St. Louis

presents

CHALLENGING CLINICAL CASE PRESENTATIONS

Five interesting/ unusual/or complex ID cases will be selected as unknowns to the audience, from area medical schools, Washington University School of Medicine, St. Louis University School of Medicine, and University of Missouri School of Medicine – Columbia.

Thursday
March 15, 2018

Engineer’s Club of St. Louis
4359 Lindell Blvd.
St. Louis, MO 63108

6:00 p.m. Reception (meet & greet)
7:00 p.m. Meeting Commences

Register at: www.wustl.edu/etransact
scroll to “Infectious Diseases Society and Event Registration”

TARGET AUDIENCE
This course is directed to infectious diseases physicians, pediatricians, public health specialists, infection control specialists, epidemiologists, and those who oversee infection control programs.

MORE DETAILS
If you have any questions please call or e-mail Susan Wightman at (314) 454-8275 or wightman.susan@wustl.edu.
Jennifer Philips, MD, PhD, is the lead author on a recent study that provides insight into how Mycobacterium tuberculosis causes disease. Mycobacterium tuberculosis has afflicted humans for thousands of years and continues to cause an enormous worldwide burden of disease. Despite the availability of effective treatment regimens for the last 40 years, today still more people die from tuberculosis (TB) than any other infection. The success of M. tuberculosis depends upon its ability to grow in macrophages. Although macrophages are cells dedicated to destroying bacteria, they are the dominant cell type in which M. tuberculosis grows. How M. tuberculosis is able to convert this antimicrobial environment into a safe haven is poorly understood. Defining how M. tuberculosis undermines the very cells that are dedicated to killing it will enable new treatments that harness the host's capacity to clear the tubercle bacilli.

In their recent publication, Dr. Philips, trainees Stefan Köster, Sandeep Upadhyay, and others, discovered that M. tuberculosis undermines the antimicrobial arsenal of macrophages by disabling the macrophage NADPH oxidase. Normally during bacterial and fungal infections, the NADPH oxidase is recruited to cellular compartments containing the microorganism, where it generates reactive oxygen species that kill the invader. The research team found that the M. tuberculosis protein, CpsA, blocks recruitment of NADPH oxidase to the host compartment containing mycobacteria. Thus, bacterial CpsA prevents macrophages from generating a burst of bactericidal reactive oxygen.

The Philips lab found that impairing the NADPH oxidase has additional benefits for M. tuberculosis. Normally, reactive oxygen species generated by the NADPH oxidase stimulate a cascade of events called LC3-associated phagocytosis (LAP), which promotes bacterial degradation. By inhibiting the NADPH oxidase, CpsA also protects M. tuberculosis from killing through the LAP pathway. The team performed studies in mice and showed that when M. tuberculosis is engineered without CpsA, the NADPH oxidase and LAP pathway can actively control the infection. Moreover, the ΔcpsA mutant failed to kill immunocompromised mice. The team's work further suggests that CpsA may have evolved from an enzyme involved in bacterial cell wall integrity into an indispensable factor that M. tuberculosis uses to evade the human innate immune response. This work points to the potential of targeting CpsA and related proteins to create new drugs and vaccines.

The study was published Oct. 10th in Proc Natl Acad Sci.

Gary Weil, MD, and his international colleagues spur new WHO guidelines for disabling tropical disease.

Research led by Washington University School of Medicine in St. Louis has prompted the World Health Organization (WHO) to issue new treatment guidelines aimed at accelerating global elimination of lymphatic filariasis – a devastating tropical disease.

An estimated 120 million people worldwide are infected with lymphatic filariasis, a parasitic disease spread by mosquitoes. The disease can cause massive swelling of lymph glands in the legs and lower body, resulting in long-term disability and social stigma.

Efforts to eliminate the disease have focused on treating entire populations of people living in areas where the disease is endemic, regardless of whether they are sick or not. Such a strategy is aimed at curing existing infections and preventing new ones.

The new WHO guidelines, announced in November, recommend a three-drug treatment regimen rather than the standard two-drug combination. The guidelines are based on studies in Asia and Africa led by Gary Weil, MD, a Washington University infectious disease specialist, and his international colleagues. Their results have demonstrated that adding ivermectin to the standard combination of diethylcarbamazine and albendazole is more effective than the two-drug regimen and just as safe.

An estimated 800 million people in 53 countries live in areas where lymphatic filariasis is transmitted. Residents in many of these areas could benefit from the three-drug regimen, Weil said.

In support of WHO’s new treatment recommendation, Merck & Co. recently announced that it would expand its donation program of Mectizan (Merck’s brand of ivermectin), making the drug available to an additional 100 million people annually.

“This new treatment has the potential to significantly shorten the time required to eliminate lymphatic filariasis in many countries around the world,” said Weil, a professor of medicine and of molecular microbiology. “WHO’s recent policy change together with Merck’s expanded donation of Mectizan should aid distribution of the three-drug regimen to many millions of people in dozens of countries where people are infected with lymphatic filariasis.”

The improved effectiveness of the new treatment is projected to eliminate lymphatic filariasis in most endemic areas within three years if enough people participate by taking the medications, which are provided for free. The WHO recommends that the triple-drug combination be distributed annually in areas where the standard two-drug regimen has not been effective or has not yet begun.
The most devastating effects of lymphatic filariasis occur when the thread-like parasitic worms that cause the disease migrate from the blood into lymphatic vessels. The worms grow and mature over a period of months and can cause blockage of the flow of lymph fluid, resulting in severely swollen legs, a condition known as elephantiasis, and genitals. Recent estimates suggest that about 35 million people are disfigured by the disease.

Washington University has played a key role in WHO’s Global Program to Eliminate Lymphatic Filariasis, which started in 2000 and provides treatment to about 500 million people annually. Weil’s earlier research led to an improved diagnostic test for the infection that is part of the global program.

An $8 million grant last year from the Bill & Melinda Gates Foundation allowed Weil and his colleagues to evaluate the safety and efficacy of the triple-drug treatment with studies of more than 23,000 people in India, Haiti, Indonesia and Papua New Guinea. The foundation recently awarded Weil’s research team an additional two-year, $2.2 million grant to continue to study the impact of this new treatment.

“The global program has made great progress since its inception in 2000, but many countries have a long way to go to eliminate lymphatic filariasis,” Weil said. “With this new approach to treatment and continued effort and support, we are optimistic that the global health community can permanently rid the world of this disease.”

This research is funded by the Bill & Melinda Gates Foundation.

Budge and Rao team up with international partners to test portable 3D scanner to assess patients with elephantiasis

device measures swollen limbs faster, more easily than other methods

An estimated 120 million people in tropical and subtropical areas of the world are infected with lymphatic filariasis; of these, almost 40 million have genital disease or elephantiasis (massive swelling of lymph glands in the legs and lower body). Health-care workers rely on leg measurements to assess the severity of the condition. However, measuring legs that are severely swollen often proves cumbersome and impractical.

But now, scientists at Washington University School of Medicine in St. Louis, working with collaborators in Sri Lanka, have shown that a portable scanning device can measure limb enlargement and disfigurement faster and more easily in patients with elephantiasis. The research tool makes it easy to obtain accurate measurements and determine whether treatments to reduce swelling are effective.
3D scanner continued

“This is important because it will allow doctors and researchers to take very accurate limb measurements in developing nations, where there are often limited tools to monitor swollen limbs,” said senior author Philip J. Budge, MD, PhD, an assistant professor of medicine in the Division of Infectious Diseases at Washington University.

In patients with elephantiasis, the parasitic worms that cause the disease make their way into the lymphatic system and prevent the lymph vessels from working properly, which leads to swollen legs. This condition also is referred to as lymphedema.

“Unfortunately, the medication does not usually reverse lymphedema in those already affected,” Budge said. “The ability to get these measurements rapidly will make it much easier to treat patients, including those in clinical trials exploring better treatment therapies.”

The device is essentially an infrared sensor, mounted on an iPad, that produces a highly accurate, virtual 3-D reconstruction of the legs using scanning technology similar to that found in Microsoft’s Xbox Kinect video game system. It was created by Atlanta-based startup LymphaTech to measure lymphedema that sometimes develops in cancer patients after lymph nodes are removed during surgery.

After learning about the technology, Washington University researchers Budge and Ramakrishna Rao, PhD, an associate professor of medicine, teamed up with international partners to test the device on 52 patients with varying stages of lymphedema at a clinic in Galle, Sri Lanka. Working with physicians at the clinic, the team compared scanner results with results from two other techniques frequently used to ascertain the severity of elephantiasis: use of a tape measure, and water displacement.

Tape measures allow researchers to measure limb circumference near the knees, feet and ankles. However, Budge said, the method can be difficult to standardize and unreliable in assessing leg volume because of bumpy, uneven skin surfaces caused by the swelling.

The water displacement procedure entails patients submerging a leg in a water tank and then measuring how much water is displaced. Each leg is done separately. “This is the gold standard for measuring limb volume, but it is cumbersome and impractical to use in field studies,” Budge said. “Some patients have lymphedema so severe, they have difficulty getting a leg into the water tank or standing still long enough for all the water to drain out. Or they may have open wounds that complicate the process.”

The study showed that the infrared scanner provided measurements of leg volume and of limb circumference at multiple points that were just as accurate and precise as those obtained by tape measure and water displacement. “But the most encouraging news is that the scanner produced highly accurate results in only...
Key malaria parasite findings could lead to new treatments

resistance to malaria drugs a growing problem

Sebastian Nasamu, MS, an MD/PhD student at Washington University School of Medicine in St. Louis, battled successive bouts of malaria as a child growing up in Ghana. He survived – but decided long ago to commit himself to eradicating the disease. The possibility that his work could lead to a treatment is the reason he goes to the lab every day.

The pursuit has led the School of Medicine’s Nasamu, Daniel Goldberg, MD, PhD, and colleagues to the identification of two crucial enzymes in the malaria parasite’s arsenal: one helps the microbe invade red blood cells; the other aids the parasite’s escape from the cells so it can move on to infect other cells.

Further, the researchers showed that a drug that cures malaria a fraction of the time of the other tests,” Budge said.

Researchers found that the average time required for scanner measurements of both legs was 2.2 minutes. In comparison, the tape measure and water displacement methods took an average of 7.5 minutes and 17.4 minutes, respectively.

“The scanning tool also offers convenience,” Budge said. “Many patients with swollen limbs often have great difficulty traveling from their homes to the clinic to have their measurements taken. The scanner should make it possible to take extremely accurate limb measurements in the patients’ homes or villages, without cumbersome equipment or inconveniencing patients.

“To our knowledge, this is the first time that infrared 3-D scanning technology has been used in patients with filarial lymphedema,” he added. “It worked so well that it has been added as a measurement tool in a future clinical trial in which we are collaborating.”

That study is a two-year, multisite, international clinical trial to determine whether the antibiotic doxycycline can reduce the severity of swelling and disfigurement in patients with lymphatic filariasis. Enrollment for Washington University’s partner site in Sri Lanka will start soon.

by Kristina Sauerwein

This study was published Oct. 5, 2017.


in mice works via one of these enzymes. The findings – published Oct. 27 in the journal Science – suggest that targeting such enzymes could lead to new kinds of anti-malarial drugs, which are urgently needed as resistance to current drugs continues to spread.

“We identified enzymes that appear to be central for invading and bursting out of red blood cells, and showed that they are targets of anti-malarial inhibitors,” said senior author Goldberg, the David M. and Paula L. Kipnis Distinguished Professor of Medicine.

An estimated 212 million people contracted malaria in 2015, and more than 400,000 – mostly children under age 5 – died of it. The disease is spread by the bite of a blood-sucking mosquito. Parasites in the mosquito’s saliva slip into a person’s bloodstream and destroy red blood cells.

“When I was growing up I had malaria maybe 30 times, two or three times a year,” recalled Nasamu, the study’s first author. “You get sick, your mom goes to the drug store, buys a couple of pills, you take them. With luck, within three days you’re feeling better, and within a week you’re back up and can go to school.”

As a child, Nasamu probably was treated with chloroquine. Today, so many malaria parasites are resistant to chloroquine that the drug is no longer useful in Africa. Instead, the drug of choice is artemisinin. “There is a massive international effort to develop new anti-malarials, but all the top prospects are based on artemisinin, and now resistance to artemisinin is spreading,” said Goldberg, who is also a professor of molecular microbiology. “If artemisinin fails, there’s not much else in the pipeline.”

In an effort to find new drugs to battle the deadly disease, Goldberg, Nasamu and colleagues have been working their way through a group of 10 parasite enzymes known as plasmepsins, trying to find the ones the parasite relies on to cause disease.

They finally hit pay dirt with plasmepsins IX and X. By inactivating the genes for the two enzymes, they found that the enzymes are indispensable in getting the parasites into and out of red blood cells. The parasites without plasmepsin X were able to invade red blood cells and multiply inside them, but then found themselves trapped. The parasites that lacked plasmepsin IX had the opposite problem: They burst out from red blood cells but were unable to penetrate the next round of cells. These were the enzymes the researchers had been looking for. Invading and exiting red blood cells are crucial steps in the life cycle of the malaria parasite. A drug that blocks this step would stop the parasite in its tracks.

Goldberg, Nasamu and colleagues screened compounds...
known to work on enzymes similar to plasmepsins in search of ones that could inhibit plasmepsin IX or X. They found three that prevent the parasite from multiplying, including one that cured malaria in mice. These compounds had been developed by the Center for World Health and Medicine at Saint Louis University. But nobody knew which enzymes the compounds targeted.

The researchers exposed malaria parasites to each compound and then allowed the microbes to infect red blood cells. Parasites treated with the compounds behaved just like parasites that lacked plasmepsin X: They wriggled impotently inside red blood cells, unable to get out. Further experiments confirmed that the three compounds target plasmepsin X.

Even though one of the compounds has proven effective in mice, developing it as a potential anti-malarial drug for people probably will require some tweaking to its chemical structure to maximize safety and effectiveness. But knowing that it targets plasmepsin X should speed that process up considerably, the researchers said.

“If you don’t know what the target is and you’re trying to make a better drug, all you can do is try changing the molecule bit by bit, randomly, and hope it works,” Goldberg said. “If you know what the target is, and you know how the compound interacts with the enzyme, you can do a much smarter job of choosing chemical modifications.”

This compound is particularly appealing because parasites seem to have difficulty acquiring resistance to it. “People have tried to induce resistance to this compound in the laboratory, and no one has been able to do it,” Goldberg said. “That doesn’t mean it can’t happen, but it’s a good sign.”

That possibility drives Nasamu. “I would like to be able to contribute to the eradication of this disease because the people who suffer the most are the people I come from,” Nasamu said. “I easily could have died of this before I was 5. But instead, I am here.”

By Tamara Bandari · October 27, 2017

Plasmepsins IX and X are essential and druggable mediators of malaria parasite egress and invasion.

Our mission is to provide outstanding clinical care, conduct ground-breaking research, and train the next generation of leaders in academic medicine and infectious diseases.

Dr. Gerald Medoff has been among the most influential leaders in the School of Medicine in the past half century, and the contributions of Dr. Medoff to the field of medicine are clearly reflected in the quality of the School and in the extraordinary individuals he has mentored. It is therefore only appropriate that we honor him by creating a fund that will provide support for young trainees and junior faculty in the Division, helping them transition their independent careers. Additionally, we rely heavily on outside donations to continue to recruit, train, and retain high quality staff to support the research, education, and clinical mission of the division.

We believe that you share our sense of pride in what we have been able to build, much of which is due to the leadership of Dr. Medoff. To make a gift online please visit our “LEADING Together” page to direct your gift to honor Dr. Medoff to the Division of Infectious Disease Fund (90991).

Thank you to our recent donors

- Dr. Hilary M. Babcock
- Dr. Ernie-Paul Barrette
- Dr. Michael H. Cynamon
- Drs. Lisa Brodsky Ring & Gregory A. Storch
- Dr. & Mrs. Lawrence D. and Nancy A. Gelb
- Drs. Daniel Eliot Goldberg & Mary Karen Cullen
- Dr. Mitsuo Kitahara
- Dr. Gary & Janice Weil

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To make a gift to the Infectious Diseases Division, you may contact Traci Albers, Division Administrator, Infectious Diseases Division, or mail your contribution. Checks can be made payable to:

Washington University School of Medicine
Infectious Diseases Division
ATTN: Traci Albers, MBA
Campus Box 8051, 4523 Clayton Ave.
St. Louis, MO 63110

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